<u>REMARKS</u>

Claims 1 – 105 have been cancelled and new claims 106 through 121 entered to more particularly point out and distinctly claim Applicants' inventions. In addition, corresponding amendments have been made to the specification. No new matter has been added. Before addressing the claims specifically, Applicants note the following features of the claimed methods and apparatus. As discussed, for example, on page 3, line 1 through page 4, line 16, there is a need in the art for an automated mass spectrometry (MS) metrology in areas such as semiconductor processing. However, traditional MS apparatus requires frequent adjustment and recalibration by skilled personnel. This frequent recalibration is required to address inevitable systematic errors introduced by instrument drift and other problems. To solve this problem, Applicants has provided an automated mass spectrometry apparatus allowing unattended and automated operation of the MS metrology tool.

This unattended use is enabled through the use of ratio measurements. Ratio measurements are reasonably immune to MS instrument drift because the change in the ratio's numerator due to MS instrument drift will also be experienced by the ratio's denominator such that both changes will cancel one another. In the same fashion, changes in the solution matrix will also not impact ratio measurements. A ratio measurement may involve an isotopic ratio measurement such as described, for example, in the paragraph beginning on page 4, line 17.

Although the use of a ratio measurement eliminated the need for frequent recalibration, that was not the only advance provided by the Applicants. In addition, Applicants
enhanced the automated ratio measurement through the use of atmospheric pressure ionization
(API) such as, for example, electrospray to create the ions analyzed by the mass spectrometer.
Unlike the relatively harsh ionization used in traditional inductively-coupled plasma mass

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spectrometers, API provides a more mild ionization that preserves species information. For example, should the species Cr(III) and Cr(VI) be ionized in an inductively-coupled plasma MS instrument, they are ionized into the same state, namely Cr(I). A MS cannot distinguish between a Cr(I) ion that was originally Cr(III) vs. a Cr(I) ion that was originally Cr(VI). So, the species information is destroyed. However, the relatively mild ionization provided by an API ionization process would not convert Cr(III) and Cr(VI) into the same ionic form. For example, suppose a sample contains CrF₃ and CrF₆. When subjected to API, such a sample will provide (CrF₂)+ ions and (CrF₅)+ ions, thereby preserving the Cr(III) and Cr(VI) species information.

Moreover, the implementation of an API ionization stage is only one feature of Applicants' invention. For example, consider the dilution module described with respect to Figure 6. As described, for example, beginning at page 30, line 19, this dilution module may be controlled to achieve a desired level of dilution selected based upon an expected concentration range of the analyte-being-characterized in the sample. As appreciated by those of ordinary skill in the art, if a mass spectrometer is being used to characterize the concentration of an analyte at the parts-per-trillion range (ppt), one would now want to use a spike having a concentration in the parts-per-trillion range (ppt). However, as noted by the Applicants, most spike solutions become unstable at concentrations of less than the ppm range. Applicants have thus cleverly provided an automated system that can, on-the-fly, dilute a relatively-concentrated-but-stable spike to the appropriate diluted concentration.

These advantageous features are reflected in the claims. To better define these advantageous features, Applicants have cancelled claims 1 through 105 and provided new claims 106 through 121. No new matter has been added. For example, consider claim 1, which now recites an <u>in-process ratio</u> mass spectrometry system. The terms "in-process" and "ratio" have been highlighted to stress the fact that Applicants' system is automated and does

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2402 MICHELSON DRIVE EUITÉ 210 IRVINE. CA 92612 (949) 752-7040 FAX (949) 752-7049 not suffer from instrument drift because it relies on a ratio measurement. Claim 1 further recites "a spike dilution apparatus configurable to dilute a spike having a first concentration to produce a processed spike having a diluted second concentration." As discussed above, such an apparatus allows the claimed system to produce an appropriately-diluted spike without suffering from the long-term stability of such a diluted spike. Claim 1 further recites a mixer, an API, and a mass spectrometer "configurable to process the ions by ratio determination." Finally, the claimed system includes a control system that configures these components such that "the sample is automatically mixed with the processed spike, ionized, and processed by the mass spectrometer, the control system being further configured to use the ratio measured by the mass spectrometer to characterize the concentration of the at least one analyte in the extracted sample."

The inventive combination recited in claim 106 stands in sharp contrast to the prior art cited in this application. For example, consider the Dahmen reference, which merely discloses a manually-operated inductively-coupled plasma (ICP) mass spectrometer apparatus configured to perform an IDMS analysis. Applicants readily admit such an apparatus is abundantly in the prior art but fail to see its relevance at making claim 106 obvious in any fashion.

Similarly, the Marchante-Gayon reference also discloses the use of a manuallyoperated ICP-MS apparatus. Applicants again readily admit such an apparatus is abundantly
in the prior art.

Just as similarly, the Rottmann reference also discloses the use of a manually-operated ICP-MS apparatus. Applicants again readily admit such an apparatus is abundantly in the prior art. Moreover, Applicants note that the "on-line" characterization of the Rottmann apparatus is misleading in that the "on-line" feature merely refers to the premixed spike being continuously pumped to one leg of a tee mixer where it is mixed with HPLC effluent and then

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sent to the ICP-MS (see, e.g., Figure 1 of this reference). Such an "on-line" feature is a far cry from Applicants' fully-automated apparatus that may be run without the need for human intervention.

The Viczian reference adds nothing further: it too discloses the use of a manually-operated ICP-MS instrument.

The published Kingston patent application and the issued Kingston patent also add nothing further: they too disclose the use of a manually-operated ICP-MS instrument. Claim 106 is thus non-obvious in view of the Kingston patent application and patent for the same reasons discussed with respect to the Dahmen reference.

The Multala reference merely discloses a mass spectrometry system in which samples from various points in a distillation column are fed continuously into a mass spectrometer.

Because no spiking is performed or suggested, the Multala apparatus could never characterize the concentration of the at least one analyte as performed by the system recited in claim 106.

Finally, the Durealt reference merely discloses a "fluidic module" configured to dilute samples. It is entirely silent with respect to the disclosure of any mass spectrometry let alone the automated ICP-MS system recited in claim 106.

Given the deficiencies noted with respect to each cited reference, Applicants respectfully traverse the Examiner's suggestions that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the various apparatus of Kingston, Durealt and Multala into the devices and methods taught by Dahmen, Merchante-Gayon, Rottmann, or Viczian because of the "automation advantages taught by Kingston, Durealt, and Multala" and the recognition that the apparatus of Dahmen, Marchante-Gayon, Rottman, or Viczian "can perform the isotope dilution analysis on a variety of samples." For example, Applicants respectfully note the Examiner has mischaracterized the Kingston reference as disclosing an automated system – it merely

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2402 MICHRISON DRIVE SUITE 210 IEVINE, CA 92612 (949) 752-7040 FAX (949) 752-7049 discloses the conventional manual operation of an ICP-MS instrument. Moreover, Applicants note that the Examiner has failed to show how each and every limitation of claim 1 has been taught or suggested by this combination of references. Indeed, the only automated MS instrument is disclosed by the Multala reference. However, this reference makes no teaching or suggestion for how to automate a mass spectrometer for the concentration characterization of analytes using a ratio measurement as recited in claim 106. With the exception of the Durealt reference, all the remaining references merely disclose the manual operation of ICP-MS instruments. In contrast, Applicants have claimed the automation of ratio measurements using an API-MS instrument, which advantageously preserves species information as discussed previously. The Durealt reference makes no mention of MS metrology whatsoever. Accordingly, claim 106 is patentable over the combination of the above-discussed references.

Claims 107 through 115 depend either directly or indirectly upon claim 106 and are thus patentable over these references for at least the same reasons. No new matter has been added. For example:

Claim 107 limits claim 106 to include a sample extraction apparatus. Support for this limitation is shown, for example, by Applicants' Figures 3 and 4 and the supporting discussion in the specification.

Claim 108 limits the sample extraction apparatus of claim 107 to be able to select from a plurality of process solutions. Support for this limitation is shown, for example, by Applicants' Figures 3 and 4 and the supporting discussion in the specification.

Claim 109 limits the system of claim 106 to include a chemical modification apparatus. Support for this limitation is shown, for example, by Applicants' Figure 3 and the supporting discussion in the specification.

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2402 MICHEL SON DRAVO SUITE 210 IRVINE. CA 92612 (949) 752-7040 FAX (949) 752-7049 Claim 110 limits the spike dilution apparatus of claim 106 to comprise a plurality of dilution sub-modules. Support for this limitation is shown, for example, by Applicants' Figure 6 and the supporting discussion in the specification.

Claim 111 limits the range of dilution achievable by each sub-dilution module of claim 110 to be from 1 to 30. Support for this limitation is shown by Figure 6, which illustrates how the spike is diluted down 30 times each dilution cycle: 1ppm to 33ppb, etc. and the accompanying discussion in the specification.

Claim 112 limits the range of dilution achievable by the system of claim 110 to encompass six orders of magnitude. Support for this limitation is again shown by Figure 6 and the accompanying discussion in the specification.

Claim 113 limits system of claim 110 to achieve its dilution by controlling flow rates. Support for this limitation is shown, for example, in the first paragraph on page 32 of the specification, which describes how the "rate of plunger travel" (and hence flow rate) may be varied to achieve a desired dilution.

Claim 114 limits the dilution mixer recited in claim 113. Support for this limitation is shown, for example, by original claim 9. Applicants note that the specification has been amended to incorporate the teachings of claim 9 as described below.

Claim 115 limits the system of claim 106 to be able to select from a plurality of spike sources. Support for this limitation is shown, for example, by Applicants' Figure 3 and the supporting discussion in the specification.

Claim 116 is a method claim that is allowable over the references analogously as discussed with respect to the system of claim 106. The act of "diluting a spike having a first concentration to produce a processed spike having a second concentration; wherein the second concentration is selected based upon an estimate of a concentration of the analyte in a sample" is supported, for example, by the discussion beginning at page 30, line 19, which

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describes the appropriate selection of a spike concentration based upon the sample concentration.

Because claims 117 through 121 depend either directly or indirectly upon claim 116, they are patentable over the art of record for at least the same reasons discussed with respect to claim 116.

No new matter has been entered analogously as discussed with respect to the dependent apparatus claims.

Applicants have amended the specification to address a number of typographical errors. In addition, the subject matter of original claim 9 has been incorporated into the specification by amending the paragraph beginning on page 32, line 8 accordingly.

With respect to the double patenting rejection over S.N. 10/094,394, (the '394 application) Applicants notes the following fundamental differences: whereas the '394 application was directed to the automated analysis of constituents, the present application is directed to the analysis of trace components. Thus, each application faces a unique set of circumstance, entailing different approaches. As appreciated by those of ordinary skill in the art, a "constituent" of a solution will exist at concentrations of approximately 1 ppm to the per cent range, such as even 30% or higher concentrations. Such concentrations will typically saturate the response of a mass spectrometer, thereby adversely affecting measurement accuracy. Thus, to analyze constituents as described in the '394 application, a technique is claimed in the '394 application of sampling a relatively-concentrated constituent that is then diluted down appropriately so that it may be spiked and analyzed without saturating the mass spectrometer. As claimed in the present application, however, it is the spike that is too concentrated, thereby requiring a spike dilution approach to appropriately dilute the sample. Accordingly, Applicants respectfully traverse the Examiner's suggestion that the claim set in the '394 application is "essentially coextensive" to that in the present application.

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CONCLUSION

For the foregoing reasons, Applicant respectfully submits that pending claims 106 – 121 are in condition for allowance.

If there are any questions regarding any aspect of the application, please call the undersigned at 949-752-7040.

I hereby certify that this correspondence is facsimile transmitted to the Commissioner for Patents, Alexandria, VA 22313-1450, at (703) 872-9306. on April 20, 2004.

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April 20, 2004 Date of Signature Respectfully submitted,

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